## REMARKS

In the specification, on page 14, the paragraph beginning on line 3 has been amended to correct minor spelling and punctuation issues.

Claim 29 has been amended. Explicit support for currently amended claim 29 is found on page 7, lines 3-25 of the specification. The amendment makes explicit that the substrates of claim 29 are limited to those which are scaffolds with edges or surfaces in close proximity to each other in the sense described on p. 7. The limitation is not narrowing as that was the scope of claim 29 by virtue of its dependency from claim 23.

Claim 33 has been amended to correct minor spelling issues.

Claim 35 has been amended to depend from claim 23, instead of from claim 32.

Claim 38 has been amended to add several polymers found in the specification e.g. at p. 11, lines 8-15. Claim 39 has been amended to add polymers found in the specification e.g. at p. 11, lines 16-21.

Claims 50-55 have been added. The substrate and formulation are described e.g. at p. 5, lines 21-22, p. 7, line 26, and p. 9, line 20. The stent is described e.g. at p. 15 and in examples 3 and 6.

Based on the present Amendment and the following Remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

**Rejection under 35 U.S.C. § 112**

Claims 23 and 29 stand rejected under 35 U.S.C. §112 as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention, as indicated in item 3 of the Office Action. The use of the term "scaffold" in claim 23 is definite and consistent with the use of the term "scaffold" on page 7 of the specification, so the rejection of claim 23 is traversed.

Currently amended claim 29 is definite and distinctly identifies the substrates of claim 29 as species of the scaffolds claimed in claim 23. The amendment makes explicit that the substrates of

claim 29 are limited to those which are scaffolds with edges or surfaces in close proximity to each other in the sense described on p. 7. Examples of such scaffolds are those having open, perforated, or mesh structures. The scaffolds according to the invention are distinct from the prior art devices without such structures referred to in the description. The rejection of claim 29 is rendered moot.

**Rejections under 35 U.S.C. § 103**

**U.S. Patent No. 5,525,348 to Whitbourne et al**

Claims 23-24, 30-40, and 43-49 stand rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 5,525,348 to Whitbourne et al., as indicated in item 5 of the office action. The examiner notes that U.S. Pat. No. 5,525,348 does not teach a loading of 100 μg of at least one therapeutic agent per square centimeter of coating, but states that this loading level would have been obvious, absent a showing of criticality.

A claim must be considered in its entirety. Independent claims 23, 43, and 45 claim a medicated device comprising a scaffold and a coating, the coating bridging from one edge or surface to another. U.S. Pat. No. 5,525,348 does not mention that the coatings can bridge from one edge or surface to another edge or surface, and does not suggest or enable such a device.

To achieve bridging in the medicated device product, the coating has specific physical properties during and following the process of making the medicated device. Such properties include viscosity and surface tension. On page 13 of the specification, it is stated that the polymer formulations containing therapeutic agent of the invention are thin, typically less than 200 micrometers (μm) in thickness. A homogeneous layer of therapeutic agent with a loading of 1000 $\mu g/cm^2$ would be expected to represent at least 10 μm of thickness; in fact, the therapeutic agent is likely to be distributed throughout the coating and have effect on the physical properties of the coating. U.S. Pat. No. 5,525,348 did not render obvious a device with a coating that bridges gaps, with high drug loading.

Independent claims 23, 43, and 45 claim loadings of 100 μg of therapeutic agent per $cm^2$ of coating. By contrast, the largest loading presented in U.S. Pat. No. 5,525,348 is in Example 16, a loading of 68 $\mu g/cm^2$. In the instant application, the claimed loadings of 100 $\mu g/cm^2$ of coating (500 $\mu g/cm^2$ in claim 24) lie well *outside of* the range of loadings presented in U.S. Pat. No. 5,525,348. High loadings are supported on page 5 and p. 12 of the specification. On page 12 of the specification, it is further indicated that a device according to the invention may contain thousands of micrograms per square centimeter. This high loading is not a mere modification of prior devices but represents a new and unexpected result beyond the range of loadings presented in the prior art.

Example 5 of the specification presents a drug loading of up to 560 μg per linear centimeter of wire. The wires were 0.0965 cm in diameter; because the wires were enclosed in a sleeve, the outer diameter was somewhat greater. Using a diameter of 0.1 cm, the circumference of the wire would be 0.3 cm. Using the given linear loading, an areal drug loading of about 1870 $\mu g/cm^2$ can be determined. A loading of 1870 $\mu g/cm^2$ is 28 times greater than the loading presented in example 16 of U.S. Pat. No. 5,525,348. Therefore, the loadings presented in the application lie far outside of the range presented in U.S. Pat. No. 5,525,348, which does not render the claimed devices obvious.

The unexpected advantage of the high loadings is the long term elution of therapeutic agent, such as paclitaxel in examples 3, 5, and 7, and the long distance elution shown in example 4. These features are explicitly recited in claims 30, 31, and 45.

**U.S. Patent No. 5,525,348 to Whitbourne et al. in view of U.S. Patent No. 6,306,176 to Whitbourne**

Claims 23-49 also stand rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 5,525,348 to Whitbourne et al. in view of U.S. Patent No. 6,306,176 to Whitbourne, as indicated in item 6 of the Office Action.

As discussed above, there are several features recited in each of the independent claims, which are neither taught or suggested by either cited reference, alone or in combination. These

include the adjacent edges or surfaces and bridging between them. The high loading of therapeutic agent is also not disclosed or suggested in either of the cited references.

In the first sentence of the last paragraph of item 6 on page 7, the Examiner states that "it would have been obvious ... to have modified the composition of Whitbourne [U.S. Pat. No. 5,525,348] by substituting PVA/VA for PVP as taught by Whitbourne [U.S. Patent No. 6,306,176] because of the expectation of obtaining similar results without undue experimentation." The relevance of this statement is unclear.

With regard to claim 42, neither U.S. Patent No. 5,525,348 nor U.S. Patent No. 6,306,176 present a coating in which both PVP/VA and an acrylate polymer are present. As discussed above, the properties of a polymer blend, such as the hybrid polymer of claim 42 can be difficult to predict from the properties of the individual polymer components. The determination of a suitable ratio of PVP/VA copolymer to an acrylate polymer to obtain a desired release rate is not obvious on its face.

In the last sentence of the last paragraph of item 6 on page 7, the examiner states that "absent unexpected results, it would have been obvious ... to have modified the composition of [U.S. Pat. No. 5,525,348] by modifying the polymeric coating to comprise a major portion of ... hydrophilic polymer materials and a minor portion of ... hydrophobic polymer materials ... to obtain a device with surfaces that show enhanced biocompatibility and a desired release rate ... as taught by [U.S. Patent No. 6,306,176]."

The Examiner appears to have misread the claims. Claim 40 reads on a coating having "at least as much" hydrophobic as hydrophilic material; i.e., equal amounts or a majority of hydrophobic material, the opposite of what the Examiner stated. Likewise, claims 41 and 42 are to a coating including a majority of hydrophobic and a minority of hydrophilic polymer.

Further, the examiner cites to no motivation to make a coating with a majority of hydrophobic and a minority of hydrophilic polymer. U.S. Patent No. 6,306,176 does not present coatings formed from blends of hydrophobic and hydrophilic polymers. The ratio in Example 1 in U.S. Pat. No. 5,525,348 is far outside the range of ratios, 1.5:1 to 7:1, presented in claims 41 and 42

of the instant application. Also, it is unclear what composition would result if the examiner combines the teachings of U.S. Pat. No. 5,525,348 and U.S. Pat. No. 6,306,176 to make an obviousness rejection. Finally, if the examiner's rejection in the last sentence of the last paragraph of item 6 on page 7 were correct and sustainable, it is irrelevant to most of the claims.

In Example 6 of the specification, Table V shows that Sample B and Sample C provided a longer and more uniform release rate of the drug than did Sample A. Samples B and C differed from Sample A in that Samples B and C contained hydrophilic polymer, ultra hydrophilic polyurethane in the case of Sample B and polyvinylpyrrolidone in the case of Sample C, whereas sample A contained no hydrophilic polymer. Sample B provided a longer and more uniform release rate than did Sample C. Sample B contained approximately equal weight percents of ultra hydrophilic polyurethane and nitrocellulose RS, a hydrophobic polymer, whereas Sample C contained a majority of hydrophobic polymer and a minority of polyvinylpyrrolidone. The data show that a minor proportion of hydrophilic material, as in the case of Sample C, can substantially change the drug elution dynamics of a polymer formulation, and that by adjusting the proportion of hydrophilic to hydrophobic polymer, the release rate characteristics of the formulation can be regulated.

Thus, the release characteristics of a coating can be tailored by varying the proportions of hydrophobic to hydrophilic polymer. The inventive devices can be designed for a specific therapy, an unexpected advantage.

All of the stated grounds of rejection have been rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is hereby invited to telephone the undersigned at the number provided.

A Notice of Allowance for claims 23-55 is respectfully requested.

Respectfully submitted,

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